CASWELL FILE 5-25-77

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY

DATE: May 25, 1977

SUBJECT: File Symbol 778-GI. SENTRY SOLID LONG LASTING HOUSEHOLD INSECTICIDE. (Naled Insecticide Strip) (Dibrom)
Miller-Morton Company, Richmond, Virginia

FROM: Toxicology Branch

TO: Mr. Franklin D. R. Gee, Product Manager # 16

Applicant seeks to register naled (Dibrom) insecticide strip. Toxicity information was furnished by reference to Chevron's Ortho files. Toxicities of the technical chemical are as follows:

Acute Oral Toxicity, rats LD_{50} = 430 mg/kg
Acute Oral Toxicity, guinea pigs LD_{50} = 197 mg/kg
Acute Dermal Toxicity, rabbit LD_{50} = 1100 mg/kg
Moderate degree of dermal irritation did not subside within 7 days
Acute Inhalation, mice Lung effects at 1.52 mg/l air at 6 hours exposure
Eye Irritation: In rabbits, Dibrom produced permanent corneal opacity, and also necrosis and scarring of the lids. No abnormalities of the lens were seen.
Demyelination Studies in Chickens, dogs, and rats: Dibrom fed at very high doses on an acute and subacute basis did not cause myelin degeneration of either the central or peripheral nervous system.

A 90-day feeding study in rats at 5, 25, & 100 ppm revealed no toxicity as measured by body weight, weight gains, food consumption, food utilization, morbidity, mortality, hematology, urine analysis, or gross or histopathologic findings.

A 90-day feeding study in dogs at 10, 30, 100, and 300 ppm revealed no toxici attributable to Dibrom as determined by growth, mortality, morbidity, hematology, urine analysis, liver & kidney function, or gross or histo-pathologic findings.

In another 90-day dog study, Dibrom was administered at levels of 0.25, 0.75; 2.5, and 7.5 mg/kg/day, and no gross manifestations of toxicity were observed It was concluded that 0.25 mg/kg/day may be considered the minimal effective dose with respect to plasma cholinesterase activity, and 2.5 mg/kg/day is the minimal effective dose for red cell cholinesterase activity.

In another 90-day study, rats received 10, 30, 100, and 300 ppm in the diet f 13 weeks. It was observed that Dibrom affects red cell activity more markedl than plasma or brain. Cholinesterase data indicate that 30 ppm of Dibrom may considered the no-effect level for rats. Regeneration rate over a 10 day recovery period was high for all three tissues examined, suggesting that Dibrom is a reversible inhibitor *in vivo*.

A 3-Generation Rat Reproduction Study at levels up to and including 25 ppm (1.25 mg/kg/day) did not reveal any abnormalities.

Dibrom and its metabolities (DDVP, dichloroacetaldehyde, and dichloroethanol) are rapidly hydrolyzed in mammals to yield no persisting tissue residues and only trace levels of the administered compounds in milk.

Studies in which Dibrom was administered to dairy cows at 1 and 10 ppm for 21 days with milk samples taken periodically during the study gave no detectable residues of Dibrom in meat or milk at 0.02 ppm sensitivity.

Standard toxicity data were requested of the applicant on the formulation to b marketed. Applicant responded by administering orally to dogs the technical material and also pellets of the formulation; the technical material produced severe and prolonged retching and vomiting, whereas the formulated pellets produced no such reaction. We would not consider this a proper study to satis the usual requirements for Acute Oral LD_{50}, Acute Dermal LD_{50}, Acute Inhalatic LD_{50}, Primary Eye Irritation, and Primary Skin Irritation. However, because o the nature of the formulation and its use, we would not consider these data necessary or applicable to the formulation.

But since use of the insecticide results in a continuous atmospheric level of the pesticide, consideration must be given to safety of this continuous exposure. The American Conference of Governmental Industrial Hygienists lists a threshold limit value for Dibrom in workroom air (for a normal 8-hour workda or 40-hour workweek) of 3 mg/m^3. The concentration of Dibrom present in the air from use of these naled insecticide strips would range from 2.3 to 32 ng/l a value of 0.1%to 1% of the acceptable threshold limit value. Even though the exposure to naled from the insecticide strip could theoretically be continuous (24 hours per day), Toxicology Branch would judge this exposure to be safe.

Also requested was teratology data on the technical chemical. These data have not yet been supplied.

RECOMMENDATION: Do not register until the data from the teratology study have been submitted and the product has been found to be non-teratogenic.

Several IBT Studies involved; Review by Dr. Gessert does not specify which, please check Tox submission and Tox studies deemed relevant are mentioned in Dr. Gessert's review. 1/9/78

Roland A. Gessert

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Toxicology Branch

1/9/78